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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,093	12/19/2001	Franz-Josef Mais	Mo6857/Le 33,762	7790
34947	7590	03/19/2004		
BAYER CHEMICALS CORPORATION PATENT DEPARTMENT 100 BAYER ROAD PITTSBURGH, PA 15205-9741				
			EXAMINER MCKENZIE, THOMAS C	
			ART UNIT 1624	PAPER NUMBER

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,093	MAIS ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10, 11 and 13-17 is/are rejected.
- 7) ☒ Claim(s) 12 and 18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is in response to amendments filed on 1/26/04. Applicant has amended the specification but made no amendment to the claims.

Specification

2. The disclosure is newly objected to because of the Applicants' amendments and the following informalities: in Example 8, page 6, the first three sentences should read, "100 parts by weight of acetonitrile, 14.5 parts by weight of 4-chloro-6-methoxypyrimidine, and 0.03 parts by weight of water were introduced into a stirred vessel and while stirring at 80°C, 37 parts by weight of hydrogen chloride gas were passed in over the course of 10 hours. An HPLC sample was then taken. This indicted that the 4-chloro-6-methoxypyrimidine was almost completely reacted and 4-chloro-6-hydroxypyrimidine had resulted." Appropriate correction is required.

In the previous amendment, Applicants replaced the wrong occurrence of 4-chloro-6-methoxypyrimidine.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

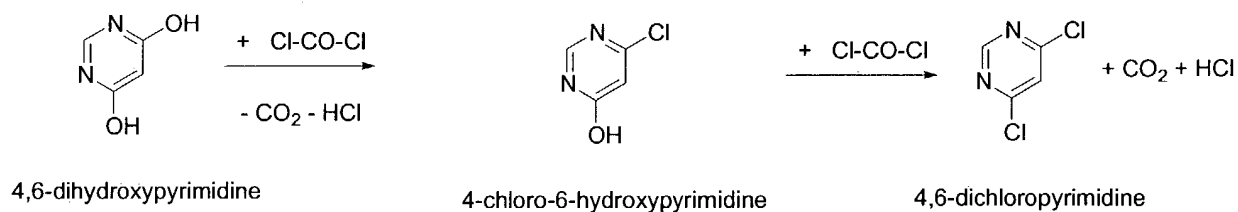
Claims 10, 11, and 13-17 remain rejected under 35 U.S.C. 102(b) as being anticipated by Bowen (WO 95/29166 A1), or, in the alternative, under 35

U.S.C. 103(a) as obvious over Bowen (WO 95/29166 A1). A process is inherently taught if inferences, which one would reasonably make, are taken into account, *In re Napier*, 34 USPQ2d 1782. The reference teaches the reaction of 4,6-dihydroxypyrimidine with phosgene to yield 4,6-dichloropyrimidine. What is inherent in this reference is the use of 4-chloro-6-hydroxypyrimidine as starting material. The MPEP says §2112, “[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection”. “There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102.” *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale will also apply to process claims claimed in terms of function, property, or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.”

The reaction of phosgene or thionyl chloride with a hydroxyl compound requires one molecule of reagent for each hydroxyl group. With phosgene, one molecule of CO₂ and one molecule of HCl must be produced as by-products in the synthesis of a chlorine derivative. Only one hydroxyl group of 4,6-

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dihydroxypyrimidine may be transformed into a chlorine atom by the phosgene reagent. The reaction taught by Bowen (WO 95/29166 A1), thus may be pictured below. Two molecules of phosgene are required in the process of Bowen (WO 95/29166 A1). Applicants' 4-chloro-6-hydroxypyrimidine starting material is a necessary intermediate in the process taught in the prior art and thus is inherently



present in the reaction mixture of Bowen (WO 95/29166 A1). Applicants' 4-chloro-6-hydroxypyrimidine starting material is generated *in situ* in the reference. Thus, claim 13, which optionally permits "a reaction mixture containing" the starting material, is inherently anticipated. Since both the starting material and product of Bowen (WO 95/29166 A1) are symmetrical, it is a random choice as to which hydroxyl group first reacts.

The process is found in paragraph 3, page 1, paragraphs 2-8, page 2, and Examples 1-6, pages 2-4 of the reference. Claims 10 and 11 require specific acid chlorides. Phosgene is an acid chloride of formula Cl-CO-Cl. Thus claims 10 and 11 are anticipated. Claims 14 and 15 require use of one equivalent of acid chloride and specific solvents. Line 26 on page 2 of the reference teaches that 2.5 to 3.6

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moles of phosgene are required for each mole of starting material. Aromatic, nitrile, ether, and polyether solvents are taught in paragraph 2 on page 2. Thus, claims 14 and 15 are anticipated. Claims 16 and 17 specify temperature and pressure. Reaction temperatures of -10 to 130°C are taught in paragraph 3, page 2 of the reference. The reference is silent as to the pressure used but since the refluxing temperature of methylene chloride is reported as 29°C in Example 2, a pressure of 1 bar may be inferred. Thus, claims 16 and 17 are anticipated.

A process claim is anticipated even if patentee of prior art did not recognize that an "inventive concept" of the new claim was necessarily present, not merely probably or possibly present, in the prior art, *Verdegaal Brothers Inc. v. Union Oil Company of California* 2 USPQ2d 1051. *Mehl/Biophile International Corp. v. Milgraum* 52 USPQ2d 1303, "[i]nherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art."

Applicants offer three new arguments supporting their assertion that the intermediacy of 4-chloro-6-hydroxypyrimidine in the reaction taught by Bowen (WO 95/29166 A1), and asserted by the Examiner as inherent in that reference, does not have the certainty of occurrence, which case law requires. Applicants offer the alternative mechanism of a termolecular reaction or a "solvent cage".

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Secondly, Applicants cite *In re Grose and Flanigen*, 201 USPQ 57, where the CCPA required, "[w]hen the PTO seeks to rely upon a chemical theory, in establishing a prima facie case of obviousness, it must provide evidentiary support for the existence and meaning of that theory." Thirdly, Applicants cite Example 1 of Bowen (WO 95/29166 A1), asserting that HPLC analysis shows the absence of the intermediate postulated by the Examiner.

Concerning the first point, a termolecular reaction means that three molecules must collide and react exactly simultaneously. In the present situation this means that two phosgene molecules and one 4,6-dihydroxypyrimidine molecule must collide together with all three molecules having the precise orientation to react. This is a total of 20 atoms, 8 from the two phosgene molecules and 12 from the 4,6-dihydroxypyrimidine. Such termolecular reactions simply do not occur in complex systems.

Fred Omega Garces (Reaction Mechanism Steps of a Reaction) writes on page 5, "[t]ermolecular mechanism (elementary step) is very rare. Scientist who propose such a mechanism must make careful measurements." Dr Rod Beavon (Rates sometimes fall) states in the sixth paragraph, that "[t]he probability of a termolecular reaction, where the three species collide simultaneously with the correct energy and the correct orientation in a single step, is very small." James A.

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Plambeck (Termolecular Reactions Are Unlikely) writes in the first two paragraphs,

"Termolecular Reactions Are Unlikely. The vast majority of elementary chemical reactions or steps are either unimolecular or bimolecular. Very few of the reactions which take place in homogeneous solutions or gas mixtures are termolecular, that is, reactions involving three molecules interacting simultaneously, and no examples of any higher molecularity than three have been found. A termolecular step can involve collisions of different or identical molecules; the general reaction can be $M + M + M \rightarrow Q$ or $M + N + O \rightarrow Q$. These collisions must be three-body collisions, since all three of the reacting molecules must be in the same place at the same time. Three-body collisions must always occur much less frequently than do comparable two-body collisions because every three-body collision is also a two-body collision but only a few two-body collisions are also three-body collisions."

W. R. Salzman (Reaction Mechanisms) writes, "[t]ermolecular reaction steps require three molecules coming together at the same time. They are rare because three-body collisions in the gas phase are rare, but there are cases of termolecular reactions in the literature."

The termolecular reactions that are known are gas phase reactions involving single atoms as one or more of the species. There are no such examples with molecules in the solution phase as complicated as are present here. The examples of termolecular reaction that do exist are the exceptions described by Dr Rod Beavon (Rates Sometimes Fall), "[c]hemistry is a complicated subject and dependent on many variables; an immense variety of compounds, reactions beyond

counting, but behind all this is a relatively small number of broad principles. However, to the fascination of people like me and the irritation of those who'd be better studying Physics, there's always the exception that tests the rule."

Solvent cages concern free-radical and solvolytic carbonium ion reactions. Solvent cages are too small to accommodate the molecules present here. Clarification is requested as to their relevance here.

Secondly, *In re Grose and Flanigen*, 201 USPQ 57 concerned an obviousness rejection concerning zeolite compounds where the CCPA upheld the rejection of the claims. The present case is an inherency rejection, not an obviousness rejection. The Examiner has made two assertions in the inherency rejection, that the reaction of phosgene with a hydroxyl group to make a chloride requires one molecule of phosgene for each converted hydroxyl group. The Examiner has also asserted that termolecular reactions in complex systems do not occur. Pauling (General Chemistry, 2nd Ed) in the first sentence mentions "law of the conservation of atoms of every element". This is a law and not a theory. Application of this law to the phosgene reactions leads to the conclusion that each molecule of phosgene reacts with a single oxygen to produce a chloro compound, one molecule of carbon dioxide and one molecule of hydrogen chloride. That is confirmed by Paquette (Encyclopedia of Reagents for Organic Synthesis) in

reaction (9) which shows the CO_2 byproduct and in the first sentence of the second column, which refers to "losing HCL". The Applicants in asserting that the reaction in the reference is termolecular must agree that two molecules of phosgene are required. The issue of termolecular reactions was discussed above.

To the third point, Bowen (WO 95/29166 A1) in Example 1 teaches, "4,6-Dihydroxypyrimidine (0.94g) was suspended in dichloromethane, dimethylaniline (1.12g) added and phosgene (5g) was then condensed into the mixture. The resulting mixture was heated at reflux for 24 hours, then cooled and poured into water. High pressure liquid chromatographic (hplc) analysis of the resulting organic layer showed a 4,6-dihydroxypyrimidine: 4,6-dichloropyrimidine ratio of 39:58." Bowen (WO 95/29166 A1) is reporting a ratio, not the absolute yield. The numbers 39 and 58 add to 97. What is the missing 3%? The reference is silent as to the presence or absence of the 4-chloro-6-hydroxypyrimidine. The reference did not look for 4-chloro-6-hydroxypyrimidine. The reference may or may not have considered its presence. None of the examples in the reference report a 100% yield, the remaining material is not accounted for.

Allowable Subject Matter

4. Objection remains to claims 12 and 18 as dependant upon a rejected claim.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


Conclusion

6. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please

direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

7. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact Mukund Shah, SPE of 1624 at (571)-272-0674.

TCMcK 


Mukund Shah
Supervisory Patent Examiner
Art Unit 1624